Actin and dynamin2 dynamics and interplay during clathrin-mediated endocytosis.

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Public Summary:
Clathrin-mediated endocytosis (CME) is a key process enabling cells to internalize extracellular material to effect growth, differentiation and development. CME involves the recruitment of numerous proteins to sites on the plasma membrane with prescribed timing to mediate specific stages of the process. Using genome editing to express fluorescent fusion proteins at native levels and live-cell imaging with single-molecule sensitivity, we explored the recruitment and interaction of the proteins dynamin2 and actin during CME. Our results demonstrate precise temporal and quantitative regulation of the dynamin2 recruitment influenced by actin polymerization, and suggest a mechanism whereby extracellular matrix stiffness and actin cytoskeleton may influence CME.

Scientific Abstract:
Clathrin-mediated endocytosis (CME) involves the recruitment of numerous proteins to sites on the plasma membrane with prescribed timing to mediate specific stages of the process. However, how choreographed recruitment and function of specific proteins during CME is achieved remains unclear. Using genome editing to express fluorescent fusion proteins at native levels and live-cell imaging with single-molecule sensitivity, we explored dynamin2 stoichiometry, dynamics, and functional interdependency with actin. Our quantitative analyses revealed heterogeneity in the timing of the early phase of CME, with transient recruitment of 2-4 molecules of dynamin2. In contrast, considerable regularity characterized the final 20 s of CME, during which approximately 26 molecules of dynamin2, sufficient to make one ring around the vesicle neck, were typically recruited. Actin assembly generally preceded dynamin2 recruitment during the late phases of CME, and promoted dynamin recruitment. Collectively, our results demonstrate precise temporal and quantitative regulation of the dynamin2 recruitment influenced by actin polymerization.